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# **Case Report**

## **MANAGING UNCERTAINTY IN OBESITY**

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# ARTICLE INFO ABSTRACT

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#### Key Words:

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Cocaine- and amphetamine-regulated transcript (CART), 'Adipokines',

#### Are we ignorant about our own health? Managing uncertainty in obesity? Diseases in the overweight is the growing health issue around the world and is reaching epidemic proportions in some nations. Body fat represents stored energy, and obesity occurs when the homeostatic mechanisms controlling energy balance become disordered. In developed countries, there is a common nutritional disorder in which there is an accumulation of excess body fat. Clinically, obesity is present when body mass index exceeds 30.It occurs when energy intake exceeds energy expenditure. Obesity is most commonly due to overeating than the caloric requirements. Obesity can be encountered with other diseases namely certain metabolic disorders, and endocrine disorders. Obesity is defined as an excess adipose tissue. Accurate quantification of body fat requires sophisticated techniques not usually available in clinical practice. Physical examination is usually sufficient to detect excess body fat. Physical examination is usually sufficient to detect excess body fat. Physical examination is usually sufficient to detect excess body fat. Reducing fat might not be as "heart-smart" as it sounds.

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## **INTRODUCTION**

Obesity is the most common metabolic problem in industrialized countries. In the USA, 32% of adults are classified as overweight, and 22.5% of these individuals are obese.(.1) Both overweight and obese subjects are at an increased risk for cardiovascular diseases(2) obesity also has serious social and psychological consequences, and affects all ages and socioeconomic groups (3)The successful management of obesity is possible through lifestyle changes in diet and physical activity alone than gastrointestinal surgery and pharmacological interventions.(4) One of the natural molecules known to prevent or retardate oxidation is -lipoic acid ( -LA) thus, the lipoic acid/dihydrolipoic acid (LA/DHLA) redox couple has received considerable attention(5) Obesity is a global epidemic disease and is recognized as a major public health problem in India. There is an immediate need to treat the issue as Obesity is the major causative factor for many noncommunicable diseases. (6)

The main function of carnitine in the body is facilitation lipid oxidation by transporting long-chain fatty acids into the inner mitochondria region where they undergo  $\beta$ -oxidation (7). Since acylCoAs cannot cross cell walls, carnitine comes into place to help with the transportation through the mitochondrial wall (8) in humans, carnitine is absorbed in the small intestinal mucosa by sodium-dependent active transport and by passive transport (9). Nonesterified carnitine (NEC), acidsoluble acylcarnitine (ASAC), and acid-insoluble acylcarnitine (AIAC) concentrations were lower in the differentiated 3T3-L1

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cells. In addition, the exogenously added carnitine inhibited the increases in triglyceride and total lipid levels (10)

In humans, carnitine is absorbed in the small intestinal mucosa by sodium-dependent active transport and by passive transport (11) In blood, carnitine does not need protein for a carrier, and is present in the free or acylcarnitine form.(12) Stress and emotional brain networks foster eating behaviors that may lead to obesity. Stressors, by activating a neural stress-response network, bias cognition toward increased emotional activity and degraded executive function. (13) The increased amount of perceived stress experienced by individuals in modern society affects feeding behavior (14) In fact, a recent study showed that sadness favored eating of high fat/sweet, hedonically rewarding foods, whereas intake during a happy state favored dried fruit (15). Elevated stress hormones and palatable food intake and the consequent accretion of fat may serve as feedback signals that reduce perceived stress (16). Leptin as a key fat hormone that stimulates secretion of the anorexigenic and sympatheticstimulatory neuropeptides and inhibits secretion of the orexigenic and parasympathetic-stimulatory neuropeptides. (17,18) Childhood obesity is a risk factor for a number of chronic conditions including the metabolic syndrome and cardiovascular diseases(19) Its prevalence increased rapidly from the mid-1980s in developed countries, although there is evidence that in the late 1990s and early 2000s, it reached a plateau or a small decrease occurred.(20).

#### History

Hippocrates wrote that "Corpulence is not only a disease itself the harbinger of others" (22)The Indian but surgeon Sushruta (6th century BCE) related obesity to diabetes and heartdisorders(24) He recommended physical work to help cure it and its side effects. For most of human history, mankind struggled with food scarcity. (23) It was common among high officials in Europe in the middle Ages and the Renaissance (25) as well as in Ancient East Asian civilizations. (26) Tobias Venner is credited with being one of the first to refer to the term as a societal disease in a published English language book. (27) It was realized that the military and economic might of nations were dependent on both the body size and strength of their soldiers and workers (32).

During the 20th century, as populations reached their genetic potential for height, the weight began increasing much more than height, resulting in obesity. In the 1950s increasing wealth in the developed world decreased child mortality, but as body weight increased heart and kidney disease became more common (28) During this time period, insurance companies realized the connection between weight and life expectancy and increased premiums for the obese. (22)Many cultures throughout history have viewed obesity as the result of a character flaw. The obese or fat character in Ancient Greek comedy was a glutton and figure of mockery. During Christian times the food was viewed as a gateway to the sins of sloth and lust. (21) In modern Western culture, excess weight is often regarded as unattractive, and obesity is commonly associated with various negative stereotypes. People of all ages can face social stigmatization and may be targeted by bullies or shunned by their peers. (29)

The weight that is viewed as an ideal has become lower since the 1920s. This is illustrated by the fact that the average height of Miss America pageant winners increased by 2% from 1922 to 1999, while their average weight decreased by 12 % (30)On the other hand, people's views concerning healthy weight have changed in the opposite direction. In Britain, the weight at which people considered themselves to be overweight was significantly higher in 2007 than in 1999. (31) These changes are believed to be due to increasing rates of adiposity leading to increased acceptance of extra body fat as being normal. (31)

Obesity is still seen as a sign of wealth and well-being in many parts of Africa. This has become particularly common since the HIV epidemic began some attribute the Venus figurines to the tendency to emphasize fertility while others feel they represent "fatness" in the people of the time. This continued through much of Christian European history, with only those of low socioeconomic status being depicted as obese. (21)

During the Renaissance, some of the upper class began flaunting their large size, as can be seen in portraits of Henry VIII of England and Alessandro dal Borro. Rubens (1577– 1640) regularly depicted full-bodied women in his pictures, from which derives the term Rubenesque. (33) During the 19th century, views on obesity changed in the Western world. After centuries of obesity being synonymous with wealth and social status, slimness began to be seen as the desirable standard (21)

#### Significant Gap in Research

At the beginning of 20<sup>th</sup> century, it was observed that patients with damage to hypothalamus tended to gain weight. In the 1940s, it was also shown that discrete lesions in the hypothalamus of rodents caused them to become obese. As early as 1953, Kennedy proposed, on the basis of experiments on rats, that a hormone released from the adipose tissue acted on the hypothalamus to regulate body fat and food intake. It is also observed that mice could become obese as a result of mutations in certain genes At least five of these are characterized including the ob (Obesity) tub (tubby) fat and ab (diabetes) genes. Mice that are homozygous for mutant forms of these genes ob/ob mice and db/db mice-eat excessively, have low energy expenditure, become grossly fart and have numerous metabolic and other abnormalities.(34)Most of the obese patients are asymptomatic. When obesity is marked, exertionaldyspnea, depression and easy fatigability are likely to occur. Marked obesity may be associated with alveolar hypoventilation leading to C02 retention which may account for the above features In obese patients Pink striate are commonly seen on abdomen, thighs, buttocks, breasts, particularly in young women. When obesity is massive exertional dyspnea and tachypnea may be seen. Intertrigo is quite common in the folds below the breast and in the inguinal regions. Sometimes systemic hypertension may be present due to associated disorders like D M. (35). Obesity can be encountered with other diseases namely certain metabolic disorders, and endocrine disorders. Obesity is defined as an excess adipose tissue. Accurate quantification of body fat requires sophisticated techniques not usually available in clinical practice. Physical examination is usually sufficient to detect excess body fat. (36)Obesity is the most common metabolic problem in industrialized countries. In the USA, 32% of adults are classified as overweight, and 22.5% of these individuals are obese. (37)

#### Major Advances and Discoveries

The discovery of functions of the distributed cell groups of corticotrophin-releasing factor (CRF) neurons, the motor neurons for activation of the pituitary and adrenal, as well as the tight interrelationships between calories, body weight, energy stores, and the HPA axis have occasioned revisions in our thinking.(38) The obese and overweight subjects who are doing regular physical activity require extra L-Carnitine for the transport of fatty acids which are used for energy production.(39)Tuft's University scientists recently put 11 middle-aged men and women volunteers on a variety of average, reduced and low-fat diets, which provided only 15% of fat from calories (a diet so strict it 's almost impossible in a real-life situation) did you have a positive effect on blood cholesterol and triglyceride levels. But a reduced-fat diet, a more realistic way of eating, only affected those levels if accompanied by weight loss. In fact, the investigators concluded, cutting fat without losing weight actually increased triglyceride levels and decreased high-density lipoproteins (HDLs) - the "good" cholesterol that helps protect against heart disease. Eat fat for a healthier body. So while excess fat isn't healthy, fat isn't a dirty word. Without some fat-soluble vitamin (including A, D, E, and K). Certain fats, like olive oil and the omega-3 fatty acids found in salmon, may help prevent heart disease. And most people say a little simply makes food taste, look and smell more.(40)Excess adiposity (obesity) and excess body weight are associated with increased incidence of several of the most important diseases of humans, including type 2 diabetes, dyslipidemias, cardiovascular disease, hypertension, And cancer. Obesity is defined as an accumulation of adipose tissue that is of sufficient magnitude to impair health.

#### Ideas where the research go next?

Scientists have discovered the precise brain mechanism that causes the body to hold onto fat, raising hopes of a cure for obesity. For the first time, lab trials have explained how the brain's ability to sense insulin in the body, levels of which are raised after a meal, is coordinated with expending or conserving energy. Researchers at Monash University in Australia have described the findings as "very exciting", and said they highlight targets for potential fat-inhibiting medicines for people who cannot help putting on weight.(41)Recent evidence suggests that development of obesity involves hormones and neurotransmitters (such as leptin, cocaine- and amphetamine-regulated transcript (CART), and ghrelin) that regulate appetite and energy expenditure. These hormones act on specific centers in the brain that regulate the sensations of satiety. Mutations in these hormones or their receptors can lead to obesity. (42) The endogenous IL-6 prevents obesity and enhances glucose tolerance (Wallenius et al 2002, Nat Med 8:75, cited more than 500 times in WoS). We also showed evidence that this effect is exerted at the level of the CNS and involves increased leptin sensitivity. We have shown that IL-6-/- mice have reduced endurance and energy expenditure during exercise (Fäldt et al 2004, Endocrinology 145:2680). These results suggest that the increase in muscle-derived IL-6 observed in plasma of experimental animals and humans is necessary for normal exercise capacity. We found that the levels of IL-6 in CSF differs in many ways from CSF leptin. I found evidence that CSF IL-6 is locally produced rather than serum derived. Moreover, body fat-regulating regions in the CNS may be exposed to insufficient IL-6 levels in more severely obese humans (43)Obesity is a major public health problem in developed countries and an emerging health problem in developing nations such as India. Globally, the World health Organization estimates that 2015, 700 million adults Will be obese. In certain countries, obesity coexists with malnutrition in individual families.

#### Current Debate

The best way to predict the future is to create it. Complications of obesity. Obesity has adverse effects on both mortality and morbidity. Changes in mortality re difficult to analyze due to the confounding Effects of lower body weight in cigarette smokers. However, it is clear that the lowest mortality rates are seen in Europeans in the BMI range 18.5-24 kg/m2 (and at lower BMI in Asians). It is suggested that obesity at age 40 years can reduce life expectancy by up to 7 years for nonsmokers and by 13 years for smokers. Coronary heart disease is the major cause of death but cancer rates are also increased in the overweight, especially colorectal cancer in males and cancer of the gallbladder, biliary tract, breast, endometrium and cervix in females. Obesity has little effect on life expectancy at > 70 years, but these obese do spend a greater proportion of their active life disabled. Epidemic obesity has been accompanied by an epidemic of type 2 diabetes and osteoarthritis, particularly of the knee. Although an increased body Size results in greater bone density through increased mechanical stress, it is not certain whether this translates to a lower incidence of osteoporotic fractures. Obesity may have profound physiological consequences, compounded by stigmatization of the obese in many societies. Body fat distribution for some complications of obesity, the distribution rather than the absolute amount of excess adipose tissue appears to be important. Increased intra-abdominal fat causes central (abdominal' 'visceral' 'android' or apple-shaped') obesity, which contrasts with subcutaneous fat accumulation causing 'generalized' ('ganoid' or pear-shaped) obesity; the former is more common in men and is more Closely associated with type 2 diabetes, the metabolic syndrome and cardiovascular disease. The key difference between these depots of fat may lie in their vascular anatomy, with intraabdominal fat draining into the portal vein and thence directly to the liver. Thus many factors which are released from adipose Tissue (including free fatty acids; 'adipokines', such as tumor necrosis factor- $\alpha$ , adiponectin and resist in; and steroid hormones) may be at higher Concentration in the liver and hence induce insulin resistance and promote type 2 diabetes.(44)

#### **CONCLUSION**

At its simplest level, obesity is a disease of caloric imbalance that results from an excess intake of calories that exceeds their consumption by the body. However, the pathogenesis of obesity is complex and incompletely understood. Ongoing research has identified intricate humoral and neural mechanisms respond to genetic, nutritional, environmental, and physiologic signals, and trigger a metabolic response through the stimulation of centers located in the hypothalamus. There is little doubt that genetic influences play an important role in weight control, but obesity is a disease that depends on the interaction between multiple factors. After all, regardless of genetic makeup, obesity would not occur without intake of food. (45) The majority of the drugs approved to treat obesity have short-term indications of usage. However, some of the newer medications approved for short-term usage are the anorexiants phentermine and diethylpropion. There is a much larger list of anorexiants used off-label for weight loss; the lipase inhibitor, orlistat, has been available for several years, and other lipase inhibitors are being considered for approval. Recently, a serotonin agonist, lorcaserin, and a combination drug, phentermine and topiramate, were also approved for the treatment of obesity. Drugs for obesity are considered effective if they demonstrate at least a 5% greater reduction in body weight as compared to placebo (no treatment).

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